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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/968,208	11/12/1997	RUSSELL HIGUCHI	9397	8271

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PATTI SELAN, PATENT ADMINISTRATOR
APPLIED BIOSYSTEMS
850 LINCOLN CENTRE DRIVE
FOSTER CITY, CA 94404

EXAMINER

SNAY, JEFFREY R

ART UNIT	PAPER NUMBER
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1743

54

DATE MAILED: 05/22/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

08/968,208

Applicant(s)

HIGUCHI, RUSSELL

Examiner

Jeffrey R. Snay

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 February 2002.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 30-47 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 30-47 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other:

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1. The drawings are objected to under 37 CFR 1.83(a) because they fail to show the apparatus as described in the specification. Any structural detail that is essential for a proper understanding of the disclosed invention should be shown in the drawing.

MPEP § 608.02(d). The specification describes a fluorometer for detection of fluorescence emission from each of a plurality of reaction tubes (page 14). The specification further describes the reaction vessels being "light sealed", e.g. by a clear or translucent cap. It is noted that the limitation of the vessels being in a sealed condition is also present in the claims. The specification further mentions the provision of a light source and an optical system that "moves the excitation light from the source to the reaction tube." All of these structural details would have been essential for a proper understanding of the disclosed invention, and none are depicted in the drawings. A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

2. The drawings are objected to under 37 CFR 1.83(a). The drawings must show every feature of the invention specified in the claims. Therefore, the following structural elements and limitations must be shown or the feature(s) canceled from the claim(s).

a. The structural relationship between the optical system and the thermal cyclor such that the detector of the optical system is "operable to detect an optical signal ... with the reaction vessel in a sealed condition."

b. The reaction vessel in a sealed condition.

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- c. The sealed transmission path (claim 36).
- d. The fiber optic cable (claim 37 and claim 46).
- e. The computer controller (claim 38 and claim 47).
- f. The reaction vessel including a clear or translucent cap optically coupled to the detector by a sealed light transmission path (claim 45).

No new matter should be entered.

A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 30-33, 36-42 and 45-47 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the provision of a fluorescence detector, does not reasonably provide enablement for the provision and use of any other "optical system" to "detect an optical signal related to the amount of amplified nucleic acid". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

5. Claims 30-47 are rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. The use of the apparatus in which elements are critical or essential to the practice of the invention, but not included in the claim(s) is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976). Specifically, the provision of an excitation light source, optical communication means between the thermal cycler and detector, and reaction vessels (the vessels being omitted as structural elements from claims 30-38) are all considered essential elements in the use of the claimed apparatus for monitoring a nucleic acid amplification reaction.

With respect to all of the above-stated rejections under 35 U.S.C. 112, first paragraph, it is noted that the extent of the originally filed specification which is available for support and enablement of the claimed apparatus is limited to the disclosure found at page 14, line 1, through page 15, line 6, and page 28, line 25, through page 29, line 9.

6. Claims 30-47 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification fails to describe what structure would have been associated to the optical system such that the

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detector would be "operable to detect an optical signal ... over a multiple-cycle period" or to "sample optical signal values over multiple thermal cycles". For example, the specification fails to describe how any excitation light source would have been constructed and coordinated with a detector to operate as claimed. The specification contains no description of detecting a signal over a multiple cycle period. The specification further fails to describe and support the claimed feature of the detector to "distinguish the detected signal from any other optical signals originating in the reaction vessel". The specification further fails to describe the presently recited feature of the thermal cyclers being computer-controlled.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 30-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Each of claims 30-38 includes a limitation on the optical system, i.e. that the system is operable to detect a signal while the reaction vessel is in a sealed condition, which is clearly dependent upon the particular reaction vessel. However, the reaction vessel is not recited as a structural element of the claim, and therefore the limitation on the optical system is of indeterminate scope.

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9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. Claims 30-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haff (1989) in view of Mackay (EP 0266881) and Schnipelsky et al ('297).

The reasons for this rejection are as set forth in the last Office action.

12. Applicant's arguments filed 02/26/02 have been fully considered but they are not persuasive. ***

Applicant argues that Haff et al teaches away from the present invention because they teach running replicates of a reaction mixture to allow different aliquots to be removed after different numbers of cycles. Applicant does not, however, suggest how this disclosure of Haff et al "teaches away" from the present invention. The fact that the disclosure of a reference is in some way different from what is claimed does not

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establish that reference as teaching away. The examiner has recognized the differences between Haff et al and the claimed invention and has fully addressed such differences under the guidelines of 35 U.S.C. 103.

Applicant further argues that Haff et al differs in that they teach the use of an autosampler to transferring a reaction mixture mixed with a dye solution to a fluorimeter. Applicant appears to argue here that the automated transfer of sample between a pcr reaction vessel and a fluorimeter, as taught by Haff et al, is not the same as applicant's claimed invention of providing an optical detector operable while the reaction vessels are in a sealed condition. The examiner concurs on this point, the modification to Haff et al to perform the fluorimetric analysis on line and in a sealed vessel condition are provided by the secondary references as detailed in the grounds of rejection.

Applicant further argues that Mackay fails to remedy the deficiencies of Haff et al because the former does not discuss temperature control, does not suggest a thermal cycler for amplification of nucleic acids, and does not detect a signal over multiple cycles while the vessel remains in a sealed condition. Similarly, Applicant argues that Schnipelsky et al does not teach performing nucleic acid amplification using a thermal cycler in conjunction with an optical system to detect a signal over a multiple cycle period. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

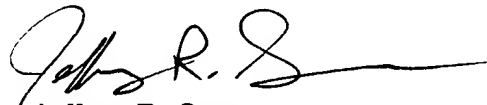
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13. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey R. Snay whose telephone number is (703) 308-4032. The examiner can normally be reached on Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill A. Warden can be reached on (703) 308-4037. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9310 for regular communications and (703) 872-9311 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0661.



Jeffrey R. Snay
Primary Examiner
Art Unit 1743

jrs
May 20, 2002